

Crossover limits have been increased. See HELP CROSSOVER for details.

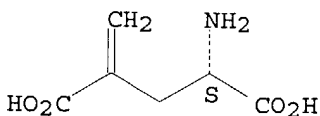
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> s 4-methylene-l-glutamic acid/cn
L1 1 4-METHYLENE-L-GLUTAMIC ACID/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 16804-57-2 REGISTRY
CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, 4-methylene-, L- (8CI)
OTHER NAMES:
CN γ -Methylene-L-glutamic acid
CN γ -Methyleneglutamic acid
CN **4-Methylene-L-glutamic acid**
CN 4-Methyleneglutamic acid
CN L- γ -Methyleneglutamate
CN L-4-Methyleneglutamic acid
FS STEREOSEARCH
MF C6 H9 N O4
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS,
CASREACT, CHEMINFORMRX, EMBASE, IPA, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA Caplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
(Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical
study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

77 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
77 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

7.04

7.69

FILE 'CAPLUS' ENTERED AT 12:09:18 ON 22 AUG 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 22 Aug 2004 VOL 141 ISS 9
FILE LAST UPDATED: 20 Aug 2004 (20040820/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 16804-57-2/prep
77 16804-57-2
3186554 PREP/RL
L2 10 16804-57-2/PREP
(16804-57-2 (L) PREP/RL)

=> s 12 and pyroglutam6
6 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> s 12 and pyroglutam?
4094 PYROGLUTAM?
L3 3 L2 AND PYROGLUTAM?

=> d 1-3 ibib abs hitstr

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:392435 CAPLUS
DOCUMENT NUMBER: 140:375488
TITLE: Process for synthesizing L-methyleneglutamic acid and analogs
INVENTOR(S): Kochat, Harry; Chen, Xinghai; Wu, Ye; Huang, Qiuli; Wang, Jianyan; Gerusz, Vincent
PATENT ASSIGNEE(S): Bionumerik Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039314	A2	20040513	WO 2003-US33236	20031022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
US 2004106826	A1	20040603	US 2003-627484	20030725
PRIORITY APPLN. INFO.:			US 2002-421489P	P 20021025
			US 2003-627484	A 20030725

OTHER SOURCE(S): CASREACT 140:375488

AB A process for synthesizing 4-methylene-L-glutamic acid and analogs comprises converting (2S)-**pyroglutamic** acid or a derivative to a 4-enamine derivative, hydrolysis to a 4-hydroxymethylene derivative, reduction to a

4-methylene derivative, and treatment with strong base to effect ring cleavage. In the examples, L-pyroglutamic acid was C/N-protected and reacted with DMF diisopropyl acetal to form intermediate Et 4-[(dimethylamino)methylene]-N-(tert-butoxycarbonyl)-L-pyroglutamate, which was converted into 4-methylene-L-glutamic acid hydrochloride.

IT 16804-57-2P

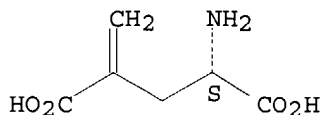
RL: SPN (Synthetic preparation); PREP (Preparation)

(process for synthesizing L-methyleneglutamic acid and analogs)

RN 16804-57-2 CAPLUS

CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:631298 CAPLUS

DOCUMENT NUMBER: 121:231298

TITLE: Efficient synthesis of 4-methylene-L-glutamic acid and its cyclopropyl analog

AUTHOR(S): Ezquerro, Jesus; Pedregal, Concepcion; Mico, Irene; Najera, Carmen

CORPORATE SOURCE: Cent. Invest. Lilly S. A., Valdeolmos, 28130, Spain

SOURCE: Tetrahedron: Asymmetry (1994), 5(5), 921-6

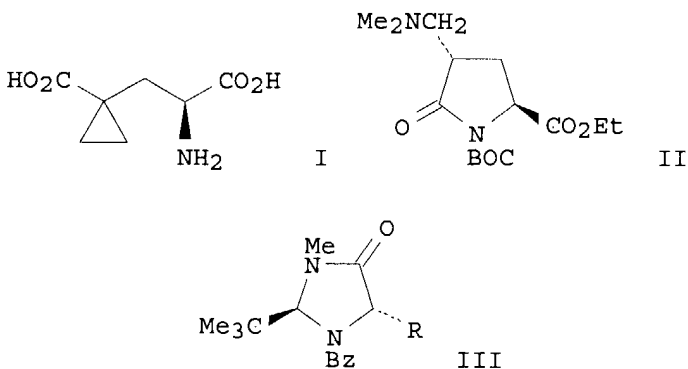
CODEN: TASYE3; ISSN: 0957-4166

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 121:231298

GI



AB Title compds. L-NHCH(CO2H)CH2C(CO2H):CH2 and cyclopropyl analog I were obtained from protected pyroglutamate Boc-pGlu-OEt (Boc = Me3CO2C) in 2 and 3 steps, resp. Key methylenepyroglutamate intermediate II was prepared by reaction of the protected pyroglutamate lithium lactam enolate with Eschenmoser's salt. Cyclopropyl derivative I was also prepared from imidazolidone III (R = H) in 3 steps. The intermediate III [R = CH2C(CO2Bu):CH2] was obtained by diastereoselective reaction of the lithium enolate of III (R = H) with Bu (2-tosylmethyl)acrylate.

IT 16804-57-2P, 4-Methylene-L-glutamic acid

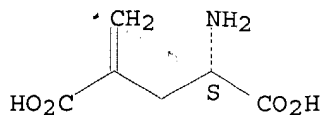
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, from pyroglutamic acid)

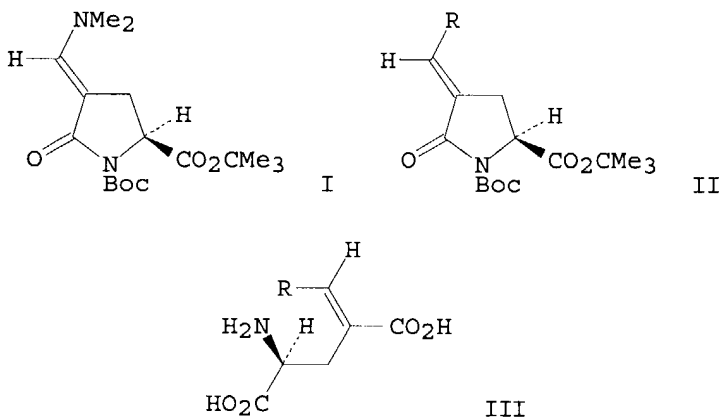
RN 16804-57-2 CAPLUS

CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

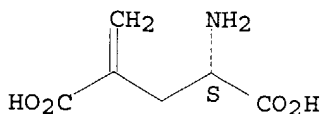


L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1993:671664 CAPLUS
 DOCUMENT NUMBER: 119:271664
 TITLE: Synthesis of naturally occurring 4-alkylideneglutamic acids
 AUTHOR(S): Moody, Claire M.; Young, Douglas W.
 CORPORATE SOURCE: Sch. Chem. Mol. Sci., Univ. Sussex, Falmer/Brighton, BN1 9QJ, UK
 SOURCE: Tetrahedron Letters (1993), 34 (29), 4667-70
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 119:271664
 GI



AB Enaminone I (Boc = Me₃CO₂C) reacted with Grignard reagents RMgBr (R = Me, Et, Ph, C.tplbond.CH) to afford (E)-alkylidene derivs. II. II (R = H, Me, Et) were converted to 4-alkylideneglutamic acids III (R = H, Me, Et).
 IT 16804-57-2P
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)
 RN 16804-57-2 CAPLUS
 CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



=>

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> SET NOTICE DISPLAY 1

NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND
SET COMMAND COMPLETED

=> D ACC 121:231298 ALL

THE ESTIMATED COST FOR THIS REQUEST IS 6.37 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

ANSWER 1 CASREACT COPYRIGHT 2004 ACS on STN

AN 121:231298 CASREACT

TI Efficient synthesis of 4-methylene-L-glutamic acid and its cyclopropyl analog

AU Ezquerra, Jesus; Pedregal, Concepcion; Mico, Irene; Najera, Carmen

CS Cent. Invest. Lilly S. A., Valdeolmos, 28130, Spain

SO Tetrahedron: Asymmetry (1994), 5(5), 921-6

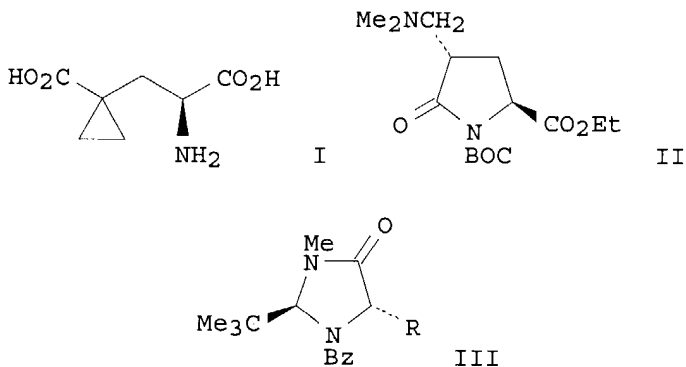
CODEN: TASYE3; ISSN: 0957-4166

DT Journal

LA English

CC 34-2 (Amino Acids, Peptides, and Proteins)

GI



AB Title compds. L-NHCH(CO₂H)CH₂C(CO₂H):CH₂ and cyclopropyl analog I were obtained from protected pyroglutamate Boc-pGlu-OEt (Boc = Me₃CO₂C) in 2 and 3 steps, resp. Key methylenepyroglutamate intermediate II was prepared by reaction of the protected pyroglutamate lithium lactam enolate with Eschenmoser's salt. Cyclopropyl derivative I was also prepared from imidazolidone III (R = H) in 3 steps. The intermediate III [R = CH₂C(CO₂Bu):CH₂] was obtained by diastereoselective reaction of the lithium enolate of III (R = H) with Bu (2-tosylmethyl)acrylate.

ST asym synthesis methyleneglutamic acid; cyclopropyl analog methyleneglutamic acid; cyclopropyl glutamic acid

IT Asymmetric synthesis and induction
(of methyleneglutamic acid and its cyclopropyl analog from protected pyroglutamate)

IT 97-88-1, Butyl methacrylate

RL: RCT (Reactant); RACT (Reactant or reagent)
(addition-elimination of, with toluenesulfinate, (tosylmethyl)acrylate from)

IT' 33797-51-2, Eschenmoser's salt
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (alkylation by, of pyroglutamate enolate)

IT 101055-56-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (deprotonation and alkylation of, with (tosylmethyl)acrylate)

IT 144978-12-1, N-tert-Butoxycarbonylpyroglutamic acid ethyl ester
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (enolate formation and alkylation of, with Eschenmoser's salt)

IT 158196-43-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and acidic ring cleavage and hydrolysis of, cyclopropaglutamic acid from)

IT 146137-50-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and alkylation by, of imidazolidinone enolate)

IT 158196-42-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclopropanation of)

IT 158196-44-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

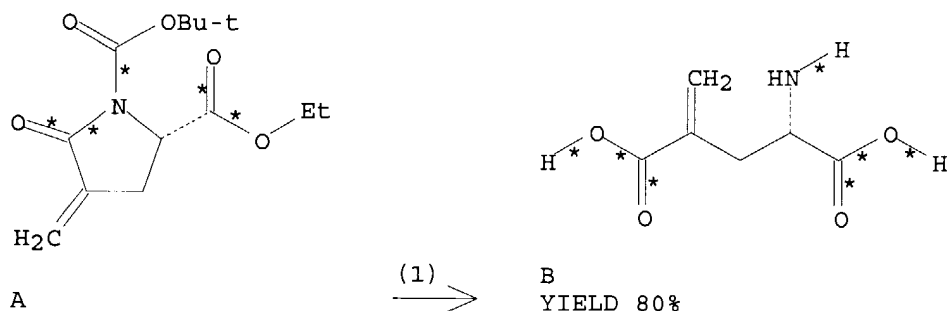
IT 16804-57-2P, 4-Methylene-L-glutamic acid 151139-87-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, from pyroglutamic acid)

IT 158196-41-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation, basic ring cleavage, and acidic hydrolysis of)

IT 158196-40-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation, cyclopropanation, or basic ring cleavage-acidic hydrolysis of)

IT 158196-39-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation, quaternization, and elimination of)

RX(1) OF 19 ...A ==> B



RX(1) RCT A 158196-40-8

STAGE(1)

RGT C 1310-65-2 LiOH

SOL 7732-18-5 Water, 109-99-9 THF

STAGE(2)

RGT D 7647-01-0 HCl

SOL 7732-18-5 Water, 109-99-9 THF

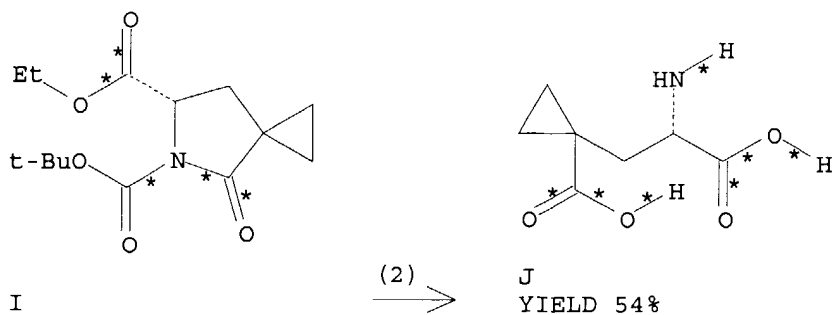
STAGE(3)

RGT E 75-56-9 Propylene oxide

SOL 67-56-1 MeOH

PRO B 16804-57-2

RX(2) OF 19 ...I ==> J



RX(2) RCT I 158196-41-9

STAGE(1)

RGT C 1310-65-2 LiOH

SOL 7732-18-5 Water, 109-99-9 THF

STAGE(2)

RGT D 7647-01-0 HCl

SOL 7732-18-5 Water, 109-99-9 THF

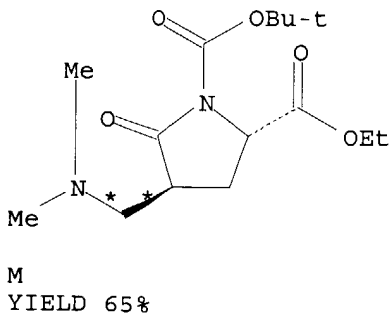
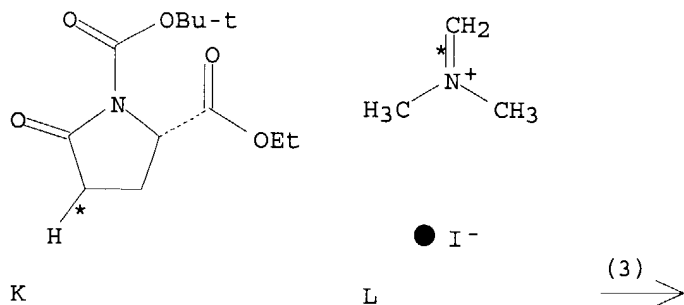
STAGE(3)

RGT E 75-56-9 Propylene oxide

SOL 67-56-1 MeOH

PRO J 151139-87-6

RX(3) OF 19 K + L ==> M...



RX(3) RCT K 144978-12-1

STAGE(1)

RGT N 4039-32-1 (Me3Si)2N.Li

SOL 109-99-9 THF

STAGE(2)

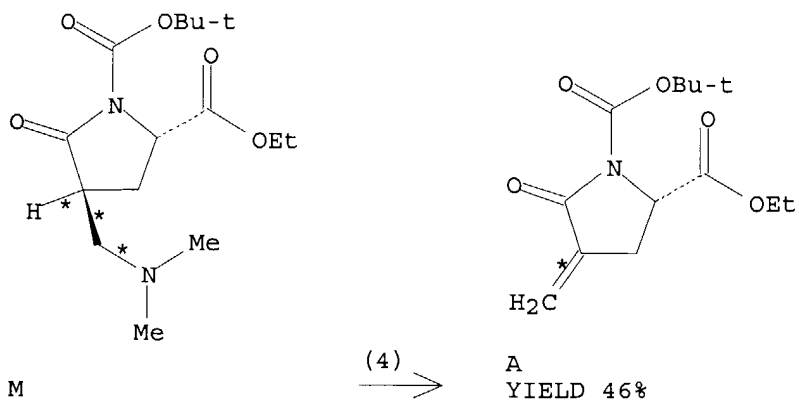
RCT L 33797-51-2

SOL 109-99-9 THF

PRO M 158196-39-5

NTE key step; stereoselective

RX(4) OF 19 ...M ==> A...



RX(4) RCT M 158196-39-5

STAGE(1)

RGT O 74-88-4 MeI

SOL 67-56-1 MeOH

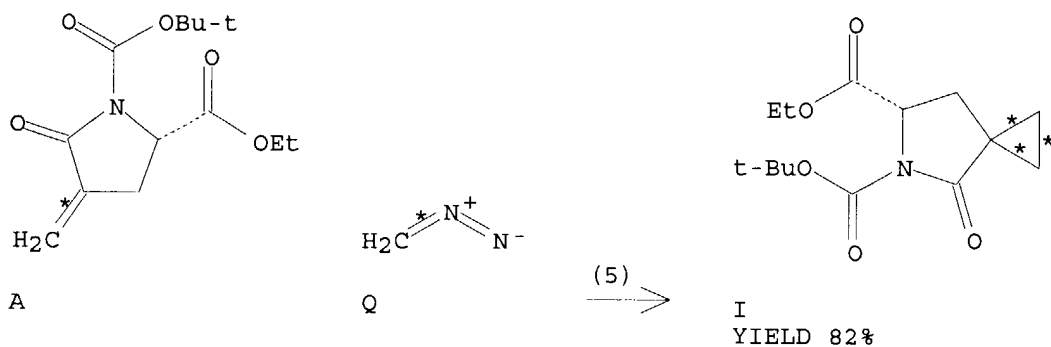
STAGE(2)

RGT P 144-55-8 NaHCO3

SOL 7732-18-5 Water

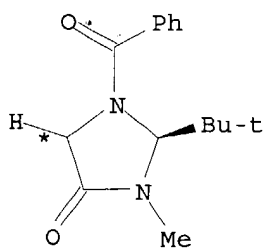
PRO A 158196-40-8

RX(5) OF 19 ...A + Q ==> I...

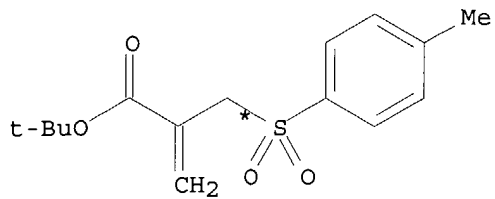


RX(5) RCT A 158196-40-8, Q 334-88-3
PRO I 158196-41-9
CAT 3375-31-3 Pd(OAc)2
SOL 60-29-7 Et2O

RX(6) OF 19 T + U ==> V...

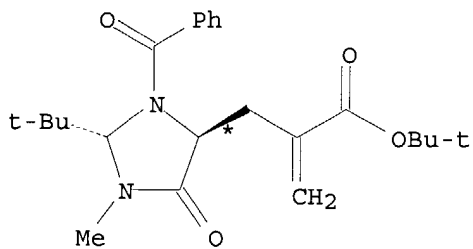


T



U

(6) →



V

YIELD 56%

RX(6) RCT T 101055-56-5

STAGE(1)

RGT W 4111-54-0 LiN(Pr-i)2

SOL 109-99-9 THF

STAGE(2)

RCT U 146137-50-0

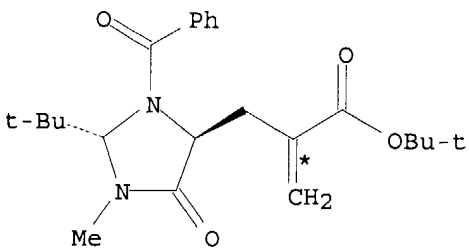
RGT X 7226-23-5 DMPU

SOL 109-99-9 THF

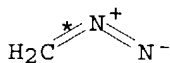
PRO V 158196-42-0

NTE key step; stereoselective

RX(7) OF 19 ...V + Q ==> Y...

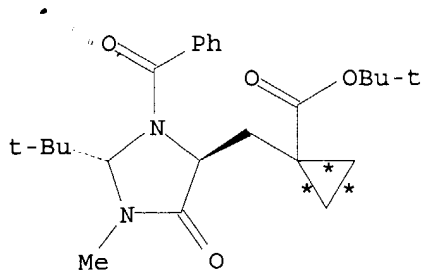


V



Q

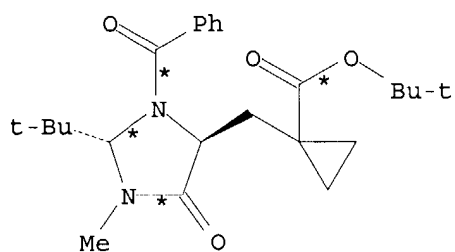
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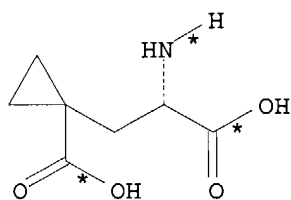
Y
YIELD 50%

RX(7) RCT V 158196-42-0, Q 334-88-3
 PRO Y 158196-43-1
 CAT 3375-31-3 Pd(OAc)₂
 SOL 60-29-7 Et₂O

RX(8) OF 19 ...Y ==> Z



Y



● HCl

Z
YIELD 97%

RX(8) RCT Y 158196-43-1
 RGT D 7647-01-0 HCl
 PRO Z 158196-44-2
 SOL 7732-18-5 Water

=> SET NOTICE LOGIN DISPLAY

NOTICE SET TO OFF FOR DISPLAY COMMAND
 SET COMMAND COMPLETED